FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) Meeting
DoubleTree by Hilton Washington DC/Silver Spring
8727 Colesville Road, Silver Spring, Maryland
May 10, 2012

DRAFT QUESTIONS TO THE COMMITTEE

1) Discuss whether the sponsor has provided an adequate response regarding:

   a. Diagnostic uncertainty for mammary tumors – i.e., adenocarcinomas versus fibroadenomas - in rats treated with lorcaserin. **(DISCUSSION)**

   b. The potential clinical risk associated with lorcaserin-induced mammary adenocarcinoma in rats (e.g., a sufficient safety margin). **(DISCUSSION)**

   c. The mechanism of action (e.g., prolactin increase) for the mammary tumors observed in rats. **(DISCUSSION)**

2) Discuss whether the sponsor has provided an adequate response regarding the potential clinical risk associated with lorcaserin-induced astrocytoma in rats (e.g., a sufficient safety margin). **(DISCUSSION)**

3) Taking into account the new in-vitro 5HT2 receptor potency data, discuss whether the phase 3 echocardiography data are sufficient to rule out a clinically meaningful increase in the risk for valvular heart disease in patients treated with lorcaserin. **(DISCUSSION)**

4) Taking into account the March 28 and 29, 2012 Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) meeting on cardiovascular risk assessment of obesity drugs, discuss the available data to assess for excess risk for major adverse cardiovascular events in patients treated with lorcaserin. **(DISCUSSION)**

5) Do the available data demonstrate that the potential benefits of lorcaserin outweigh the potential risks when used long-term in a population of overweight and obese individuals? **(VOTING)**

   a) If you voted 'Yes' to question #5, please provide your rationale and comment on the need for and approach to patient monitoring and risk management.

   b) If you voted 'No' to question #5, please provide your rationale and comment on what additional preclinical or clinical information should be required to potentially support approval.